Randomized PEG-based ABA polyether block copolymers as a non-antigenic drug delivery system

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Abstract:

Poly(ethylene glycol) (PEG) is an essential building block in modern nanomedical applications. Poloxamers are one of the most frequently used PEG-based pharmaceuticals.[1] However, a significant prevalence of anti-PEG antibodies (APAs) up to 83 % has been documented.[2] Accelerated blood clearance (ABC effect) and complement activated-related pseudoallergy (CARPA) poses a serious risk for patients treated with PEG-based nanoformulations.[3] As a novel approach, we have developed the randomized PEG (rPEG) technology, which preserves the well-established PEG structure and chemistry while significantly reducing antibody recognition.[4]

This study focused on a fully polyether-based ABA triblock copolymer system utilizing rPEG as a non-antigenic, hydrophilic A-block and hydrophobic glycidyl ethers as B-block. The ABA triblock copolymers were synthesized using living anionic ring-opening polymerization (AROP) with sequential monomer addition. The resulting rPEG-*b*-P(AnisylGE)-*b*-rPEG copolymers were employed to solubilize curcumin via the thin-film method. In conclusion, the rPEG-*b*-P(AnisylGE)-*b*-rPEG copolymers successfully demonstrate the potential of a fully polyether-based drug delivery system with significantly reduced anti-PEG antibody recognition, though improvements in micelle stability are necessary.

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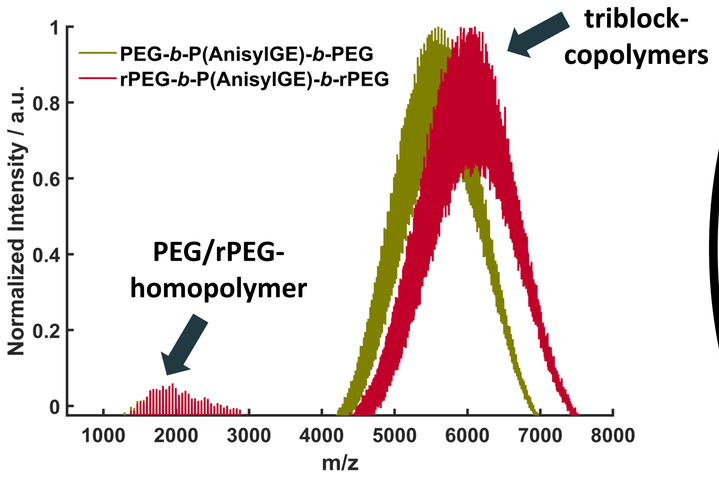
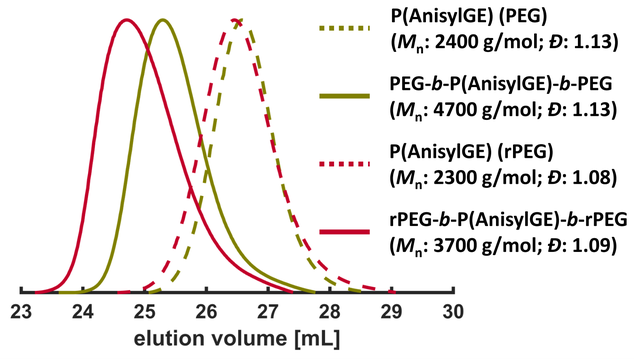
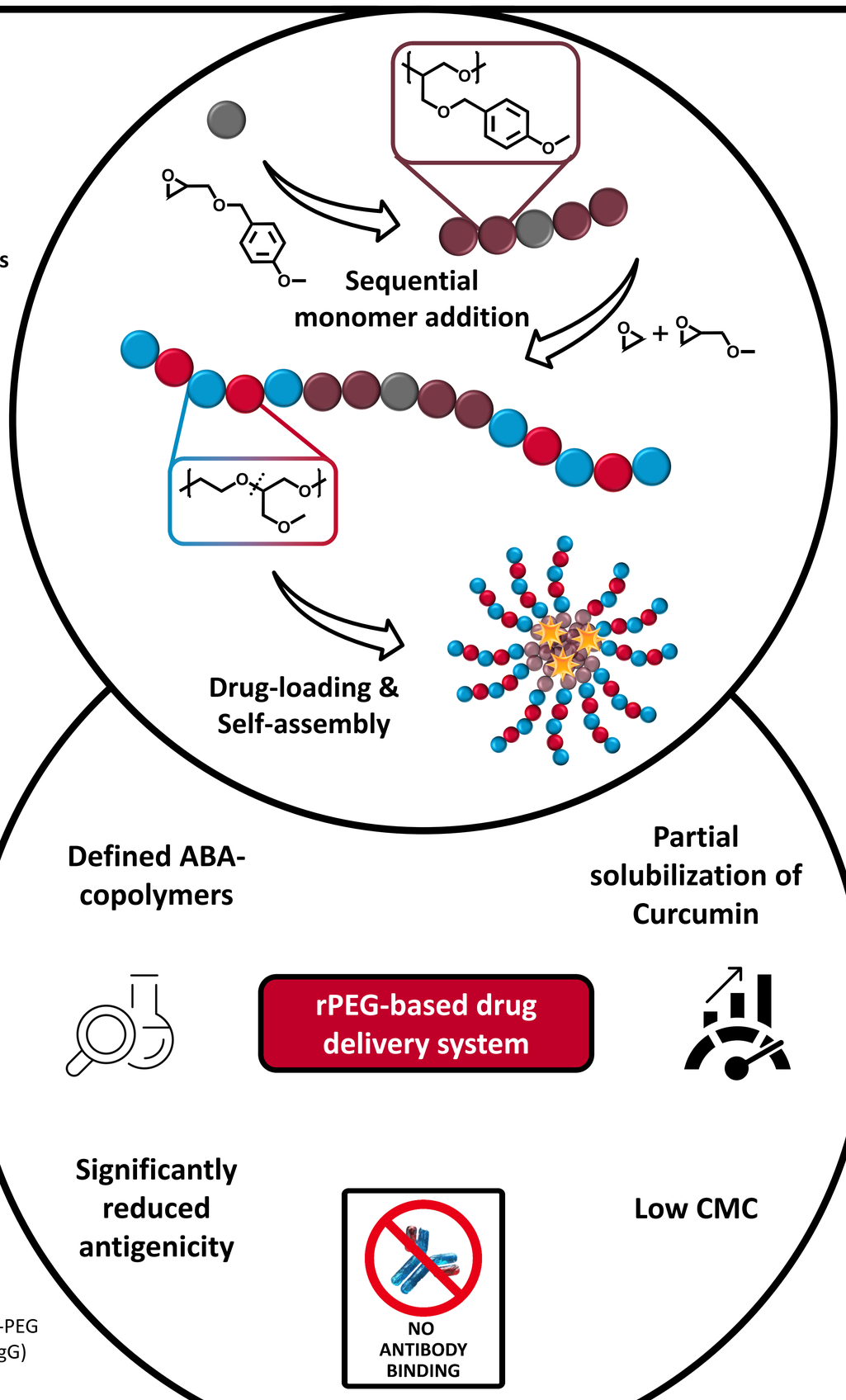
Synthesis

MALDI-ToF

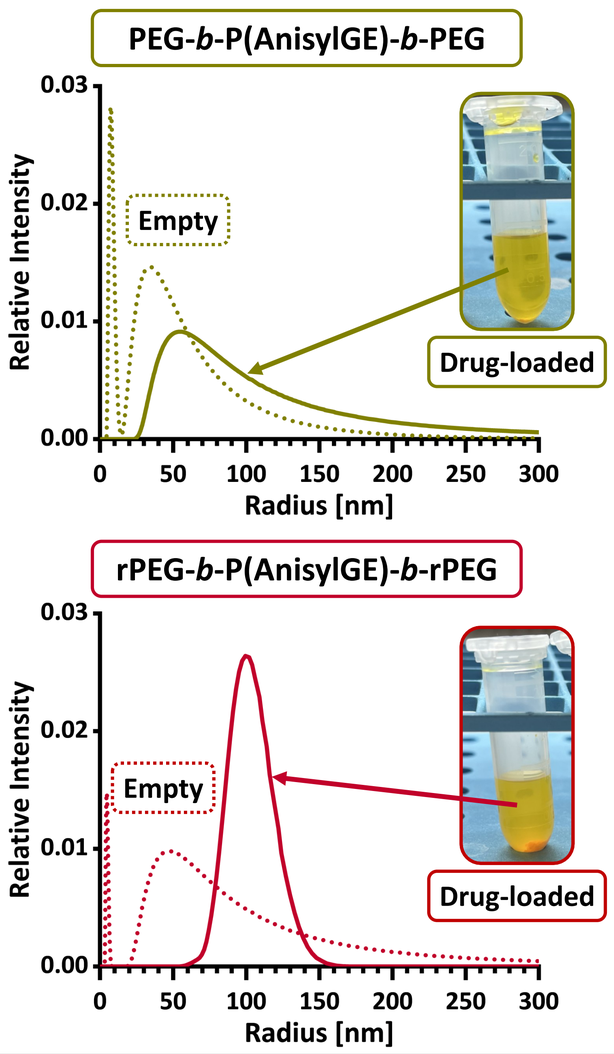


SEC-Analysis



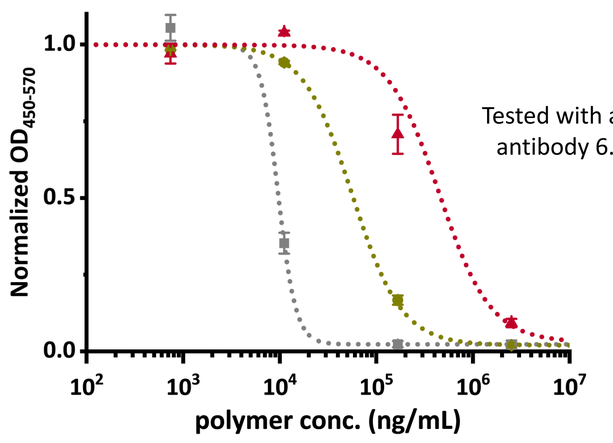


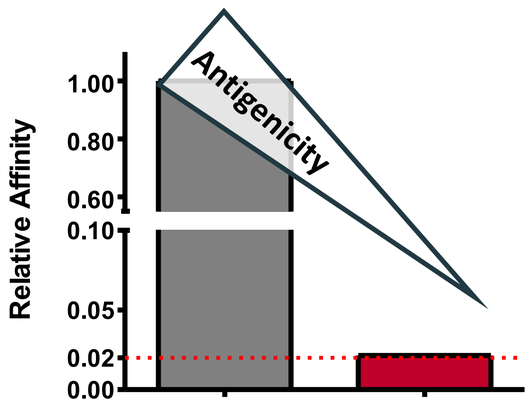
Formulation

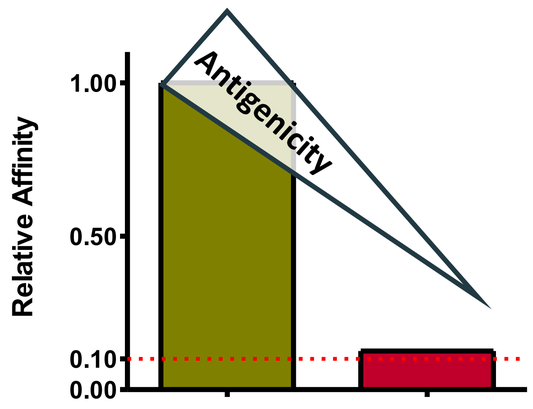


Antigenicity

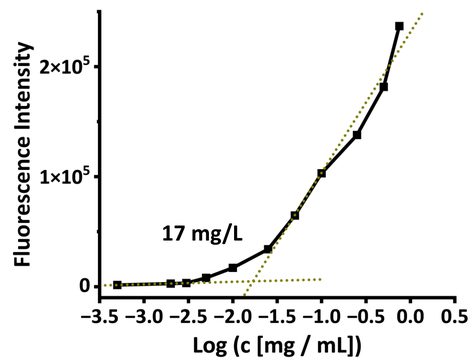
Competitive ELISA



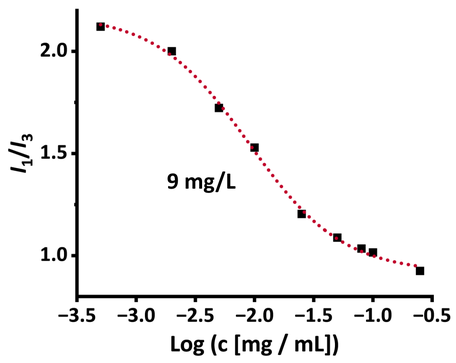


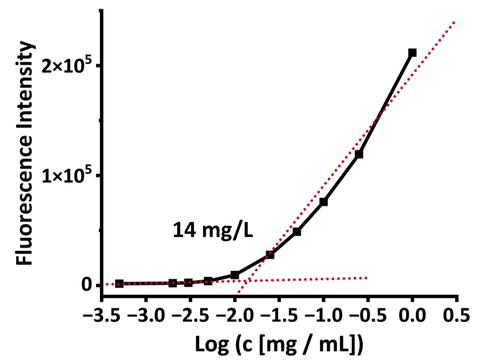


Micellization – CMC



	CMC_{Pyrene}	$CMC_{Coumarin-6}$
PEG-b-P(AnisylGE)-b-PEG	-	17 mg/L
rPEG-b-P(AnisylGE)-b-rPEG	9 mg/L	14 mg/L





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